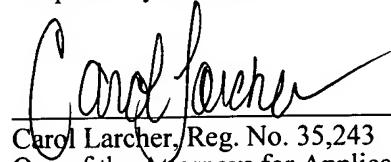


REMARKS

The title has been amended to reflect the claimed subject matter. The specification has been amended to recite the claim of priority. The claims have been amended in view of the restriction requirement in the prior application. The claims are now limited to the kit and are supported by the claims as originally filed and by the specification at, for example, page 4, line 17, through page 10, line 19, page 12, line 19, through page 13, line 29, and page 22, lines 22-31. Therefore, no new matter has been added by way of these amendments.

The application is considered in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,



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Date: November 7, 2001

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Bonner et al.

Art Unit: Unassigned

Application No. Unassigned

Examiner: Unassigned

Filed: November 7, 2001

For: A KIT FOR DETERMINING DNA  
DOUBLE-STRANDED BREAKS WITH  
ANTI- $\gamma$ -H2A ANTIBODIES

AMENDMENTS TO TITLE, SPECIFICATION AND CLAIMS  
MADE VIA PRELIMINARY AMENDMENT

Amendments to Title:

The title has been amended as follows: A KIT FOR DETERMINING DNA  
DOUBLE-STRANDED BREAKS WITH ANTI- $\gamma$ -H2A ANTIBODIES[, FUSION  
PROTEINS THEREOF AND METHOD AND KIT FOR DETERMINING DNA DOUBLE-  
STRANDED BREAKS]

Amendments to Specification:

At page 1, line 3, the following has been inserted:

CROSS-REFERENCE TO RELATED PATENT APPLICATIONS

This patent application is a divisional of copending U.S. Patent Application No.  
09/351,721, filed July 12, 1999.

The paragraph from page 6, line 25, to page 7, line 9, has been amended to read as follows:

The isolated or purified antibody or fragment thereof of the present invention specifically binds to a C-terminal phosphorylated serine in an H2A histone protein. H2A histone proteins are found in all examined species of animals. Preferably, the H2A histone protein is a mammalian H2A histone protein. More preferably, the H2A histone protein is H2AX. H2AX is one of the three types of conserved histone H2A protein species. H2AX differs from the other two H2A proteins, H2A1-H2A2 and H2AZ, by the presence of a conserved motif at the C-terminus (Mannironi et al., Nucleic Acid Research, 17, 9113-9125 (1989)). Preferably, the C-terminus of the H2A histone protein

of the present invention comprises the amino acid sequence SQ(D/E/A)(I/L/Y/F) (SEQ ID NO: 1). It is the phosphorylation of the serine in the motif, residue 139 in mammals, that yields the modified form named  $\gamma$ -H2AX.

Amendments to Existing Claims:

Claims 1-26 have been canceled.

Claims 27-34 have been added.

27. A kit for determining DNA double-stranded breaks, wherein said kit comprises (i) an isolated or purified antibody or antigenically-reactive fragment thereof that binds to a C-terminal amino acid sequence of an H2A histone protein, said C-terminal amino acid sequence consisting of SQ(D/E/A)(I/L/Y/F) (SEQ ID NO:1) that comprises a phosphorylated serine, wherein the antibody or antigenically reactive fragment thereof does not detectably bind to a C-terminal amino acid sequence of an H2A histone protein, said C-terminal amino acid sequence consisting of SQ(D/E/A)(I/L/Y/F) (SEQ ID NO:1) that does not comprise a phosphorylated serine under conditions when the isolated or purified antibody or antigenically-reactive fragment thereof binds to the C-terminal amino acid sequence of an H2A histone protein, said C-terminal amino acid sequence consisting of SQ(D/E/A)(I/L/Y/F) (SEQ ID NO:1) that comprises a phosphorylated serine, and (ii) a means of facilitating detection of binding of said antibody or antigenically-reactive fragment thereof to an H2A histone protein.

28. The kit of claim 27, wherein said phosphorylated serine is about four amino acids from the C-terminus of said H2A histone protein.

29. The kit of claim 27, wherein said fragment is selected from the group consisting of Fab, Fab', F(ab')<sub>2</sub>, and F(v).

30. The kit of claim 27, wherein said H2A histone protein is mammalian.

31. The kit of claim 30, wherein said H2A histone protein is H2AX.

[illegible]

34. The kit of claim 33, wherein said labeled secondary antibody is linked to an  
e.